IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
TRANSMITTAL

Applicants: C.C. Lambeth et al. Attorney Docket No. WEYE115226/23562

Application No: 09/618,307 Group Art Unit: 1638

Filed: July 18, 2000 Examiner: D.T. Fox

Title: POLLEN POLYMIX PLANT BREEDING METHOD UTILIZING MOLECULAR PEDIGREE ANALYSIS

Federal Way, Washington 98063
February 9, 2005

TO THE COMMISSIONER FOR PATENTS:

Enclosed are the following

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Susan J. Finn

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BRIEF - PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicants:	C.C. Lambeth et al.	Attorney Docket No. WEYE115226/23562
Application No:	09/618,307	Group Art Unit: 1638
Filed:	July 18, 2000	Examiner: D.T. Fox
Title:	POLLEN POLYMIX PLANT BREEDING METHOD UTILIZING MOLECULAR PEDIGREE ANALYSIS	

APPEAL BRIEF

February 9, 2005

TO THE COMMISSIONER FOR PATENTS:

This brief is in support of a Notice of Appeal filed in the above-identified application on December 10, 2004, to the Board of Patent Appeals and Interferences.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

FEDERAL CASES

FEDERAL STATUTES

I. REAL PARTY IN INTEREST

Weyerhaeuser Company, a Washington corporation, having a place of business at 33663 Weyerhaeuser Way South, Federal Way, Washington, is the assignee of the entire interest of the appealed subject matter.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF CLAIMS

Claims 20-31 are pending in the application. All stand rejected under 35 U.S.C. § 103(a) and under 35 U.S.C. § 112, first paragraph. Claims 20-31 are appealed. The table below indicates their status.

Claim(s)	Status	Appealed
1-19	Canceled	No
20	Original	Yes
21	Previously Presented	Yes
22	Previously Presented	Yes
23	Previously Presented	Yes
24	Previously Presented	Yes
25	Previously Presented	Yes
26	Previously Presented	Yes
27	Original	Yes
28	Amended	Yes
29	New	Yes
30	New	Yes
31	New	Yes

IV. STATUS OF AMENDMENTS

The application was finally rejected in an Office Action dated August 27, 2003. Thereafter, a Request for Continued Examination accompanied by an Amendment and Response to the final Office Action was mailed on January 27, 2004, and entered into the file. The application was again finally rejected in an Office Action dated October 18, 2004. A copy of the claims, as amended, is attached in the Claims Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

There is one independent claim on appeal, Claim 20. Claim 20 is directed to a method of tree breeding which allows the identification of elite trees for use in the next generation of tree breeding. The method involves using a mixture of pollen derived from many male parents (polymix crossing) to pollinate female reproductive structures and using DNA analysis to determine the pedigree of progeny trees. Specifically, the method comprises the steps of:

(a) mixing pollen obtained from a breeding group comprising a plurality of parental trees to obtain a pollen polymix;

(b) pollinating female reproductive structures from each parental tree in the plurality of parental trees with the pollen polymix to obtain a plurality of progeny lots, wherein each progeny lot comprises seeds obtained from a different cross between the pollen polymix and each different parental tree of the plurality of parental trees;

(c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score;

(d) determining the pedigree of a plurality of progeny trees using DNA analysis; and

(e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding.

One of the objectives in plant breeding designs is to know the full pedigree of each progeny in a cross; that is, to identify both the maternal and the paternal parent of a progeny plant (Specification, page 3, lines 1-3; page 11, lines 31-33). Knowledge of the full pedigree of a progeny plant is advantageous for several reasons. One important reason is that it allows the level of inbreeding to be controlled (Specification, page 3, lines 1-3; page 7, lines 3-7). There are many different plant breeding designs, each of which has advantages and disadvantages

(Specification, page 3, line 10, to page 7, line 33). One of these is polymix crossing (Specification, page 5, line 21, to page 7, line 7).

Polymix crossing involves mixing pollen from several males and applying it to isolated females (Specification, page 5, lines 22-23). Because pollen from several males is mixed, it is unknown which specific male is the parent of a specific progeny plant. This has been widely acknowledged to be a disadvantage in polymix breeding designs because, for example, the level of inbreeding cannot be controlled in the absence of pedigree information for a progeny plant (Specification, page 6, lines 19-21; page 7, lines 1-7; page 8, lines 2-5). The present invention overcomes this disadvantage by using DNA analysis to determine the pedigree of progeny trees in a polymix breeding design, as indicated in step (d) of Claim 20. The DNA analysis is based on the known fact that there are slight variations in the DNA sequence of individual plants belonging to the same species. These variations are typically referred to as polymorphisms or polymorphic alleles.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 20-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an adequate written description in the specification.

2. Claims 20-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an enabling description in the specification.

3. Claims 20-31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bridgwater (1992) in *Handbook of Quantitative Forest Genetics*, Kluwer Academic Pub., Dordrect, The Netherlands, pp. 69-95, in view of El-Kassaby & Ritland (1992) *Theor. Appl. Genet.* 83(6-7):752-8 and Stoehr et al. (1998) *Can. J. For. Res.* 28: 187-95.

VII. ARGUMENT

1. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 20-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an adequate written description in the specification. The Examiner has taken the position that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the Examiner, the specification does not provide guidance for the isolation or characterization of DNA from any tree species other than *Pinus taeda*, or for the isolation and characterization of any other type of DNA marker other than SSRs from any tree species other than *Pinus taeda* (Office Action mailed January 2, 2003, page 3). The Examiner also notes applicants' failure to provide a conserved nucleotide sequence which encompasses molecular markers from a multitude of unrelated tree species (Office Action mailed August 27, 2003, page 3). Applicants respectfully disagree for the following reasons.

The U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") has interpreted 35 U.S.C. §112, first paragraph, to require the patent specification to "describe the claimed invention so that one skilled in the art can recognize what is claimed." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968, 63 U.S.P.Q.2d 1609, 1616 (Fed. Cir. 2002). In evaluating whether a patentee has fulfilled this requirement, the standard is that the patent "disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Id.*

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, issued by the Patent and Trademark Office ("PTO"), state (1) that the review of whether the disclosure satisfies the written description requirement for the

claimed subject matter is conducted from the standpoint of one of skill in the art at the time the application was filed, (2) that there is an inverse correlation between the level of skill and specificity of disclosure, and (3) that information which is well known or conventional in the art need not be described in detail in the specification. 66 Fed. Reg. 1099, 1105, 1106 (Jan. 5, 2001). The written description requirement is met "if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described." *Id.* at 1106. Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. *Id.* The Federal Circuit has adopted the PTO's standard for determining compliance with the written description requirement. *Enzo*, 63 U.S.P.Q.2d at 1613.

Applicants submit Claims 20-31 are supported by an adequate written description because (a) the art of tree breeding, including the use of polymix crosses, was mature at the time the application was filed; (b) the art of DNA analysis to distinguish individual trees was mature at the time the application was filed; (c) no knowledge of DNA sequence is necessary to practice the methods of the invention; and (d) the methods of the invention do not require a correlation between a desirable trait of a plant and a DNA sequence. Accordingly, a skilled artisan would have understood based on the specification that the inventors were in possession of the claimed invention.

(A) The Art of Tree Breeding, Including the Use of Polymix Crosses, Was Mature at the Time of Filing the Application and Is Adequately Described in the Specification

Plants have been bred for desirable characteristics (referred to as "traits," "phenotypic traits," or "phenotypes"), such as disease resistance, for millennia. Many different breeding methods have been developed, including polymix breeding methods (see, e.g., Bridgwater (1992) in Fins et al. (eds.) *Handbook of Quantitative Forest Genetics,* Kluwer Academic, Dordrect, The

Netherlands, pp. 69-93, of record; Burdon & Shelbourne (1971) *NZ J. For. Sci.* 1(2):174-193, of record). The specification provides a description of numerous prior art breeding methods (Specification, page 3, line 10, to page 7, line 33). For example, the specification shows a chart that describes the common objectives of plant breeding designs (Specification, page 2, line 1, to page 3, line 9). The specification further evaluates the success of different breeding methods to accomplish these objectives (Specification, page 3, line 10, to page 7, line 33). In particular, the specification provides a detailed description of polymix breeding methods (Specification, page 5, line 21, to page 7, line 7). As defined in the specification, the term "polymix" refers to a mixture of pollen obtained from a plurality of pollen donors having different genotypes (Specification, page 11, lines 11-12). Thus, a polymix cross involves mixing pollen from several males and applying it to isolated females (Specification, page 5, lines 22-23).

Therefore, applicants submit that polymix breeding methods were well known and conventional in the art at the time of filing the application and are adequately described in the specification.

(B) The Art of DNA analysis to Distinguish Individual Trees Was Mature at the Time of Filing the Application and Is Adequately Described in the Specification

The use of DNA analysis to distinguish between individual trees of a species was well known in the art at the time the application was filed. For, example, such DNA analysis has been used for determining paternity, for estimating pollen contamination, for measuring self-pollination versus out-crossing rates, for measuring male reproductive success, and for measuring supplemental mass pollination success (for example, see Stoehr et al. (1998) *Can. J. For. Res.* 28:187-95, of record; Isagi et al. (2000) *Heredity* 84:143-51, of record; Ziegenhagen et al. (1998) *Can. J. For. Res.* 28:317-21, of record; Wheeler & Jech (1992) *New Forest* 6:311-28, of record; Cervera et al. (1996) *Plant Growth Regulation* 20:47-52, of record; Anzidei et al. (1999) in E.M. Gillet (ed), *Which DNA Marker for Which Purpose?*, of record; Nicese et al. (1998) *Euphytica*

101:199-206, of record; Chen & De Filippis (1996) *Australian Forestry* 59(1):46-55, of record; Dale & Teasdale (1997) *Proceedings of IUFRO '97 Genetics of Radiata Pine*, Rotorua, New Zealand, December 1-4, 1997, FRI Bulletin No. 203, pp. 313-317, of record; Davis et al. (1997) *Proceedings of the 24th Biennial Southern Forest Tree Improvement Conference*, Orlando, Florida, June 9-12, 1997, p. 405, of record; Nance & Nelson (1989) *Proceedings of the 20th Southern Forest Tree Improvement Conference*, Charleston, South Carolina, June 26-30, 1989, pp. 50-56, of record; Neale & Williams (1999) *Can. J. For. Res.* 21:545-54, of record; Neale et al. (1989) *Proceedings of the 20th Southern Forest Tree Improvement Conference*, Charleston, South Carolina, June 26-30, 1989, pp. 363-72, of record; Nesbitt et al. (1996) *Silvae Genet.*, April 23, 1996, pp. 6-10, of record; Richardson et al. (1997) *Proceedings of IUFRO '97 Genetics of Radiata Pine*, Rotorua, New Zealand, December 1-4, 1997, FRI Bulletin No. 203, of record; Vaillancourt et al. (1998) *Australian Forestry* 61(3):207-10, of record).

The specification provides a detailed description of DNA analysis methods and DNA markers that may be used to determine the pedigree of individual plants (Specification, page 14, line 3, to page 16, line 18). As described in the specification, DNA analysis refers to any method of analysis that reveals genotype information (Specification, page 12, lines 15-16). According to the DNA analysis methods, DNA sequence polymorphisms (i.e., variations in sequence between individual trees of the same species) are used as landmarks to track pedigree (Specification, page 12, lines 4-28; page 14, lines 3-13). The specification states that in the practice of the methods of the invention, any DNA analysis method that reveals DNA polymorphisms (i.e., differences between individual plants of the same species) between the parental plants and the progeny plants can be used (Specification, page 14, lines 11-13). The specification also notes that similar methods have been used to determine paternity in humans (Specification, page 14, lines 26-27).

Moreover, the specification provides adequate guidance for the isolation of DNA from a multitude of tree species. A working example of DNA isolation is provided in the specification using the commercially available DNeasy 96 DNA extraction kit from Qiagen (Specification, page 22, line 13, to page 14, line 4). One skilled in the art would know that the DNeasy kit is useful to isolate DNA from a wide range of plant species (for example, see pages 10-15 of Qiagen's technical bulletin, of record).

With respect to methods of DNA analysis for progeny pedigree determination, numerous examples of such methods are provided such as, for example, RFLP analysis, AFLP analysis, RAPD analysis, SSR analysis, and so on (Specification, page 12, lines 15-28; page 16, lines 8-18; page 21, line 6, to page 26, line 17; page 26, line 18, to page 31, line 19). Applicants note that the methods of DNA analysis disclosed in the specification were routine, well known in the art, and widely applicable to a variety of tree species (see, e.g., Staub (1996) *HortScience* 31:729-40, of record). Moreover, the specification provides a detailed example of the use of DNA analysis in determining paternity in loblolly pine (Specification, page 26, line 18, to page 31, line 19).

Furthermore, a description of all the possible DNA sequences that could be used in the practice of the claimed invention is impracticable because the number of polymorphisms in any tree species that could be used for the pedigree analysis is potentially infinite. For example, it has been estimated that the maize genome has up to 62 million SNPs (Mogg et al. (1999) Plant and Animal Genome VII Conference Abstract Guide, Sherago International Inc., P491, reviewed in Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001), page 3, of record). This estimate illustrates that it would not be realistic to provide a written description of every possible polymorphism in the genome of every tree species.

In addition, applicants submit that a requirement for a written description for every possible DNA sequence useful for pedigree analysis in trees would not further the policy of providing public notice of the boundaries of the claimed invention in this case. One of skill in the art would clearly be apprised that the claims encompass any form of DNA analysis to determine the pedigree of progeny plants.

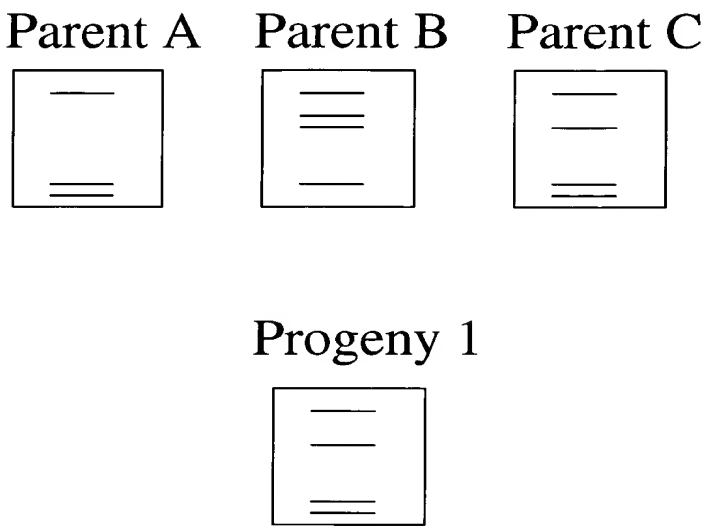
Therefore, applicants submit methods of DNA analysis to distinguish individual trees were well known and conventional in the art at the time of filing the application and are adequately described in the specification.

(C) No Knowledge of DNA Sequence Is Necessary to Practice the Methods of the Invention

The methods of the invention are directed, at least in part, to improving conventional polymix plant breeding designs, in which the paternal parent of individual progeny plants is unknown. The present invention addresses this disadvantage by using DNA analysis to determine which of the male plants whose pollen is present in the polymix is the parent of a progeny plant. As described above, DNA analysis refers to any method of analysis that reveals genotype information that can be used to track pedigree (Specification, page 12, lines 4-28; page 14, lines 3-13).

Applicants respectfully submit the following hypothetical example (of record, see response to Office Action filed July 20, 2004) to illustrate that no knowledge of the DNA sequence of parental plants or progeny plants is necessary in order to practice the methods of the invention. In this example, plants A, B, and C represent three parental plants in a breeding group that contributed pollen to a polymix (for example, step (a) of Claim 20). This polymix is used to pollinate female reproductive structures of a parental plant in the breeding group to produce progeny plants (for example, step (b) of Claim 20). Progeny 1 is one of the progeny plants whose phenotype (e.g., plant height) is evaluated (for example, step (c) of Claim 20). The DNA

analysis to determine the pedigree of progeny 1 (for example, step (d) of Claim 20) is shown in the figure below.



The figure shows bands representing fragments of DNA from parental plants A, B, and C and from progeny plant 1 separated by gel electrophoresis. Gel electrophoresis is a standard method in the art to separate differently sized fragments of DNA. Even in the absence of prior knowledge of the sequence and identity of the individual DNA bands, the DNA analysis clearly points to plant C as the parent of progeny 1 because the distribution of bands is the same for plant C and progeny 1.

Moreover, the figure above highlights that a description of all the numerous possible DNA sequences that could be analyzed in the practice of the claimed invention is neither necessary nor feasible. Any DNA sequence polymorphism can be used in the practice of the present invention. A sequence polymorphism can take the form of, for example, an insertion, a deletion, or a single nucleotide change (single nucleotide polymorphism, abbreviated as SNP). Importantly, knowledge of the actual sequence of the DNA marker or its position in the genome is typically not necessary to practice the invention. This point is further illustrated by the following example, in which DNA sequences of a DNA marker in parents A and B are arbitrarily designated to be "ACGGTA" and "ATGGTA," respectively. The sequences "ACGGTA" and "ATGGTA" are unimportant in themselves. What is relevant is that the second nucleotide is polymorphic—that is, it is *different* in these two sequences ("C" in parent A and "T" in parent B)—and that this difference is detectable by one or more methods of DNA analysis (e.g., RFLP, AFLP, sequencing, etc.). A "C" at the second nucleotide position in progeny 1 would indicate that its parent is parent A, whereas a "T" at the second nucleotide position in progeny 1 would indicate that its parent is parent B. In some embodiments of the invention, this sequence polymorphism causes a difference in size of a DNA fragment that is detectable, for example, by gel electrophoresis, as shown in the figure above. In these embodiments, the pedigree of progeny trees can be determined *without knowing any of the nucleic acid sequence of the DNA marker.*

Similarly, if the polymorphism is an insertion or a deletion of one or more nucleotides, the presence or absence of the insertion or deletion can typically be determined indirectly, without knowing the sequence of the relevant polymorphic region (e.g., by observing an increase or a decrease in the size of a band on a gel).

Applicants respectfully disagree with the Examiner's statement that DNA markers such as SSRs and SNPs require extensive sequencing, citing Krauss & Peakall (1998) *Aust. J. Bot.* 46:533-46, Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001), and Anzidei et al. (1999) in E.M. Gillet (ed), *Which DNA Marker for Which Purpose?* (Office Action mailed October 18, 2004). In fact, Edwards & Mogg explicitly point out sequencing is only one of many methods for identifying SNPs (Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001), pp. 4-7). Alternative methods described include single-strand conformation polymorphisms, chemical cleavage of mismatches, and enzyme mismatch cleavage (Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001), pp. 5-7).

Accordingly, applicants respectfully submit that knowledge of the DNA sequence of parental and progeny plants is not necessary to practice the claimed invention.

(D) No Correlation Between a Trait and a DNA Sequence is Necessary to Practice the Methods of the Invention

According to the Examiner, "[t]he invention is not merely drawn to the use of DNA fingerprinting to distinguish individuals, but is drawn to a measure of phenotype and the ability of the DNA fingerprint to be predictive of the ability of the individual to transmit particular traits to the progeny" (Office Action mailed October 18, 2004, page 3). Specifically, "[t]he Examiner maintains that the claimed invention is indeed directed to the correlation of DNA marker data

and particular traits" (Office Action mailed October 18, 2004, page 4). Furthermore, the Examiner states that Staub et al. (1996) *HortScience* 31(5):729-40 supports the Examiner's position in its teaching that marker-assisted selection is still in its infancy and is hampered by genetic interactions such as epistasis, loose linkages, and problems in accurate phenotypic classification (Office Action mailed April 20, 2004). Applicants respectfully maintain that the Examiner has mischaracterized their invention.

The genetic markers described in Staub et al. are used as "heritable entities that are associated with economically important traits" (Staub et al., page 729, Column 1, first paragraph). In other words, Staub et al. establishes links between markers and specific phenotypic traits, i.e., a specific DNA marker is always present in plants that have a particular phenotypic trait and is absent from plants that do not have that phenotypic trait. The type of analysis practiced by Staub et al. is referred to as linkage analysis or marker-assisted selection (Staub et al., page 729, Column 1, first paragraph). Often the goal of linkage analysis or marker-assisted selection is to identify a gene that causes a particular phenotypic trait.

As explained above, the methods of the invention are directed to improving conventional polymix plant breeding designs, in which the paternal parent of each progeny plant is unknown. The present invention addresses this disadvantage by using DNA analysis to determine which of the male plants whose pollen is present in the polymix is the parent of a progeny plant. Contrary to the Examiner's assertion, the invention is *not* directed to linking DNA markers with one or more phenotypic traits. Instead, DNA analysis is used merely to determine which of the plurality of parental trees represented in the polymix cross gave rise to a specific progeny tree. Referring back to the hypothetical example described in the previous section and the figure showing DNA bands from parental plants A, B, and C and from progeny plant 1, applicants respectfully point out that the distribution of bands is not in any way linked to the phenotype (e.g., plant height) of

progeny 1. It merely establishes the pedigree of progeny 1, namely that its parent is plant C. Thus, the DNA analysis used in the methods of the invention has some similarities with DNA fingerprinting to determine human parentage: the presence of a shared DNA marker may permit the inference that a particular person is the parent of a child, but it in no way indicates that a particular phenotype (e.g., blue eyes) is linked or associated with the presence of the shared DNA marker. Because the methods of the invention are not used to link DNA markers with phenotypes, the problems associated with the method of Staub et al. that were alluded to by the Examiner (e.g., epistasis, loose linkages, etc.) are not applicable to the claimed invention.

Therefore, applicants respectfully submit that the methods of the invention do not require a correlation between the presence of a desirable trait in a tree and a specific DNA sequence.

Conclusion

For the reasons provided above, applicants submit that a skilled artisan would have understood based on the specification that the inventors were in possession of the claimed invention and that Claims 20-31 are supported by an adequate written description. Applicants respectfully request reversal of this ground of rejection.

2. Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 20-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an enabling description in the specification. The Examiner alleges lack of enablement with respect to (a) the identification of molecular markers from a variety of tree species and their use to determine pedigree, (b) the phenotypic determination in a multitude of tree species, and (c) the use of polymix breeding coupled with pedigree analysis to select an elite breeding group (Office Action mailed January 2, 2003, pages 5-7; Office Action mailed August 27, 2003, pages 4-5; Office Action mailed April 20, 2004, pages 5-7; Office Action mailed October 18, 2004, pages 4-7). Accordingly, the Examiner concludes that the practice of the method would require undue experimentation. Applicants respectfully disagree with the Examiner's conclusions for the following reasons.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). The following factors are relevant in determining whether making and using an invention would require undue experimentation: the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the amount of guidance presented, the presence of working examples, and the quantity of experimentation necessary. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

In re Marzocchi, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphases in original). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is consistent with the contested statement." *Id.* at 224, 169 U.S.P.Q. at 370.

The Federal Circuit "has repeatedly explained that a patent applicant does not need to include in the specification that which is already known to and available to one of ordinary skill in the art." *Koito Mfg Co. v. Turn-Key-Tech, L.L.C.*, 381 F.3d 1142, 1156, 72 U.S.P.Q.2d 1190, 1200 (Fed. Cir. 2004). In fact, "a patentee preferably omits from the disclosure any routine technology that is well known at the time of application." *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254, 70 U.S.P.Q.2d 1321, 1325 (Fed. Cir. 2004). Thus, "[i]t is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed." *Enzo Biochem. Inc. v. Calgene*, 188 F.3d 1362, 1374, 52 U.S.P.Q.2d 1129, 1138 (Fed. Cir. 1999).

Applicants submit the claimed method does not require undue experimentation for the following reasons.

(A) The Identification of Molecular Markers From a Variety of Tree Species and Their Use to Determine Pedigree Requires No Undue Experimentation

According to the Examiner, the specification does not provide any guidance for the isolation or characterization of molecular markers other than SSRs from a single tree species, *Pinus taeda*, and the use of such markers to determine pedigree (Office Action mailed January 2, 2003, pages 5 and 7; Office Action mailed October 18, 2004, page 5). Applicants respectfully disagree.

Applicants submit that the specification contains specific guidance on the identification of markers from a variety of tree species. Molecular methods useful in the practice of the present invention allow the determination or inference of an individual's genotype based upon analysis of that individual's DNA (Specification, page 12, lines 4-14). The genotype information is then compared to all potential parent genotype information to infer the pedigree of the individual. As described above, the DNA analysis techniques disclosed in the specification were well known in the art at the time of filing (see, e.g., Staub et al. (1996) *HortScience* 31:729-40 (1996), of record).

The development and use of informative markers for pedigree analysis in a number of tree species is enabled by the specification in view of the state of the art at time of filing. The specification states that any method of molecular analysis can be used that reveals a sufficient number of genetic polymorphisms (variation in a base pair at a given site within members of the same species) to identify which parental plants are the parents of a particular progeny (Specification, page 14, lines 11-13). Further, an illustrative working example describing use of single nucleotide repeat microsatellites (SSRs) to track parentage in loblolly pine is provided as a type of marker that is useful in the practice of the method of the invention (see Specification, Examples 1 and 3-5). Specific guidance is provided in the form of primer sequences, including 7 primer pairs useful for analyzing chloroplast microsatellites and 3 primer pairs useful for analyzing nuclear microsatellites (Specification, Table 2). However, applicants note there is nothing inherently unique about loblolly pine and the disclosed markers. The methods for detecting SSR markers that are described in the specification are equally applicable to the detection of any polymorphic nucleic acid marker (i.e., nucleic acid amplification and assessment of distribution, inheritance, and variability of polymorphic markers) (Specification, page 26, line 18, to page 31, line 19). Applicants note that the primer pairs for chloroplast provided in the

specification (SEQ ID NO: 1-14), originally described by Vendramin et al. (1996) *Mol. Ecol.* 5:595-598 (of record), are known to work across a wide range of species due to the high degree of sequence conservation of the chloroplast genome. As stated in the specification, all of the 20 microsatellite primer pairs (Specification, Table 2, Example 3) used to amplify simple sequence repeat regions in the chloroplast genome of *Pinus thunbergii* were found to also amplify similar size DNA fragments in *P. taeda* (Specification, page 27, lines 20-24). Moreover, Anzidei et al. states that the same set of primers described by Vendramin et al. "have been used with success in 110 different conifer species belonging to different taxonomic classifications, in particular to the Pinaceae, Cupressaceae and Taxodiaceae" (Anzidei et al. (1999) In: *European Union DGXII Biotechnology FW IV Research Programme Molecular Tools for Biodiversity*, Gillet. E.M. ed., of record).

In addition, applicants submit that numerous DNA markers in addition to single nucleotide repeat microsatelles were well known in the art at the time of filing for many tree species, including for example, chloroplast DNA markers in Douglas fir (see e.g., Stoehr et al. (1998) *Can. J. For. Res.* 28:187-95, of record); amplified fragment length polymorphism (AFLP) markers in *Populus spp.* (see, e.g., Cervera et al. (1996) *Plant Growth Regulation* 20:47-52, of record); microsatellite markers in *Magnolia obovata* (see, e.g., Isagi et al. (2000) *Heredity* 84:143-51, of record), AFLP markers in *Persoonia mollis* (Proteaceae) (see e.g., Krauss & Peakall (1998) *Aust. J. Bot.* 46:533-46, of record), and RAPD markers in walnut (*Juglans regis L*) (see e.g., Nicese et al. (1998) *Euphytica* 101:199-206, of record). Accordingly, applicants respectfully submit that no undue experimentation is required for the identification of molecular markers from a variety of tree species and their use to determine pedigree.

i. Additional Arguments Submitted by the Examiner

a. Anzidei et al. (1999) In: *European Union DGXII Biotechnology FW IV Research Programme Molecular Tools for Biodiversity*, Gillet. E.M. ed.: The Examiner states that Anzidei et al. teach the unpredictability inherent in the use of SSR markers (Office Action mailed October 18, 2004, page 5). Applicants respectfully disagree. Anzidei et al. state that for one microsatellite marker (Pt30205), "individuals carrying the same size variants are not always characterized by the same microsatellite sequence" (Anzidei et al., page 3, penultimate paragraph). This statement in no way implies that the use of SSR markers is unpredictable. It merely shows that for one SSR marker, some polymorphisms may be missed by only looking at the size of the fragments and that some other method (such as sequencing) may be necessary to distinguish between polymorphism alleles of this marker. Moreover, Nicese et al. state that "fragment size can be considered a reliable predictor of homology among closely related individuals, as is the case in this study, although this is not necessarily true at higher taxonomic levels" (Nicese et al. (1998) *Euphytica* 101:199-206, of record, page 202, Columns 1-2). Thus, rather than teaching that the use of SSR markers is unpredictable, Anzidei et al. support the reliability of using this type of marker.

b. Nicese et al. (1998) *Euphytica* 101:199-206: The Examiner states that Nicese et al. teach that "RAPD markers are hampered by the low frequency of markers which are polymorphic or amplifiable, the high level of environmental influence thereon, the requirement for close relatedness in order to ensure accuracy, the requirement for a highly outcrossing species, the presence of markers in progeny but absence thereof in parents, the requirement for special verification steps utilizing genotype versus primer comparisons, and the requirement of larger numbers of generations of crossing and molecular markers" (Office Action mailed October 18, 2004, pages 5-6). Applicants respectfully disagree with the Examiner's characterization of

Nicese et al. For example, rather than showing that a low frequency of markers are amplifiable, Nicese et al. state that "[a]lmost all the primers yielded scorable amplification patterns (Figure 2)" (Nicese et al., page 201, Column 2). Moreover, Nicese et al. do not state that the frequency of polymorphic markers is low, but that "[t]he apparent low level of polymorphism detected (about 25% of primer pairs tested) can be explained by the strict criterion to score the markers" (Nicese et al., page 202, Column 1). With respect to the requirement for special verification steps, Nicese et al. do not refer to any such requirement but state that "[i]n order to maximize the reliability of the process, the reproducibility of the results obtained was tested in two ways" (Nicese et al., page 202, Column 2). With respect to the presence of markers in progeny but absence thereof in parents, Nicese et al. note that "most of the fragments amplified from DNA obtained from the progenies were also present in the parents" (Nicese et al., page 203, Column 1). Applicants could find no reference on the pages pointed to by the Examiner of any "environmental influence" on markers, "the requirement for close relatedness in order to ensure accuracy," or "the requirement of larger numbers of generations of crossing and molecular markers." In fact, Nicese et al. state that "[t]he results obtained, using eighteen primers that yield 23 polymorphic RAPD bands . . . , produced a unique fingerprint for each of the 19 walnut genotypes included in this study . . . allowing an unequivocal identification of each genotype (Nicese et al., page 202, Column 2; see also page 204, Column 1, stating that "the markers we have used allow us to unequivocally distinguish all the cultivars studied"). Moreover, Nicese et al. conclude that "RAPD markers can detect enough polymorphism to differentiate among walnut genotypes, even among closely related genotypes, and the genetic similarity based on RAPDs appears to reflect the known pedigree information" (Nicese et al., page 199, abstract). Thus, Nicese et al. do not support the Examiner's position that undue experimentation is needed in order to practice the methods of the invention.

c. Krauss & Peakall (1998) *Aust. J. Bot.* 46:533-46: The Examiner states that Krauss & Peakall teach that AFLP markers require highly outcrossing species, expensive equipment and high cost, and that they are hampered by unpredictability, disappearing fragments, relative lack of accuracy inherent in biallelic markers, limited recoverable information, and low repeatability (Office Action mailed October 18, 2004, page 6). Applicants respectfully disagree with the Examiner's characterization of Krauss & Peakall. Krauss & Peakall discuss both the advantages and the limitations of AFLPs (Krause & Peakall, pages 542-543), but the Examiner only focuses on the limitations. In striking contrast to the Examiner's position, Krauss & Peakall conclude that "the AFLP method produces sufficient polymorphism for the potentially unambiguous assignment of paternity in natural populations of *P. mollis*" (Krause & Peakall, page 544, conclusion). Based on their observations, Krauss & Peakall find that "it will be feasible to generate well over 100 polymorphic AFLP loci with as few as three AFLP primer pairs. This level of polymorphism is sufficient to assign paternity unambiguously to more than 99% of all seed in experiments involving small, known paternity pools" (Krause & Peakall, page 533, abstract). Thus, Krauss & Peakall support applicants' position that no undue experimentation is needed in order to practice the methods of the invention.

d. Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001): The Examiner states that Edwards & Mogg teach various limitations in the use of SNPs, including high cost, the requirement of hazardous chemicals, and the complications provided by polyploid plant species (Office Action mailed October 18, 2004, pages 6-7). Applicants respectfully disagree with the Examiner's characterization of Edwards & Mogg. Specifically, Edwards & Mogg conclude that "SNPs are well on their way to becoming the dominant marker system in commercial plant breeding" and "there is no doubt that SNPs will become the method

of choice for DNA fingerprinting" (Edwards & Mogg, page 11, conclusions). Therefore, Edwards & Mogg do not support the Examiner's position that undue experimentation is required to practice the methods of the invention.

In summary, for the reasons described above, all the references cited by the Examiner support, rather than refute, applicants' position that the identification of molecular markers from a variety of tree species requires no undue experimentation for one of ordinary skill in the art.

(B) The Phenotype Determination in a Multitude of Tree Species Requires No Undue Experimentation

According to the Examiner, the specification does not provide adequate guidance on phenotype determination in a multitude of tree species (Office Action mailed January 2, 2003, pages 5 and 7). Applicants respectfully disagree.

As an initial matter, applicants note that phenotypic evaluation has been successfully used in plant breeding for millennia. Moreover, applicants submit that the specification provides sufficient guidance in view of the state of the art to enable the method of evaluating progeny trees using objective criteria to obtain a phenotypic score as claimed. The term "phenotype score" is described in the specification as the objective measurement of any phenotypic trait or characteristic that is desirable in a plant breeding program, such as, for example, disease resistance, growth rate, growth habit, chemical composition of any plant tissue, drought resistance, temperature hardiness, elevation adaptation, fecundity and breeding value (see, e.g., Specification, page 10, lines 27-32; page 13, lines 22-25). The term "objective criteria" is described as the measurement of any plant characteristic or phenotype with any detection or measurement device that provides statistically meaningful data regarding the characteristic or phenotype being measured (see, e.g., Specification, page 10, lines 23-36). In addition, methods are provided for statistical analysis of breeding values and heritability determinations (see, e.g., Specification, page 13, lines 20-30).

Further, a working example is provided describing the measurement of exemplary phenotypic traits including height growth, stem diameter growth, straightness, disease resistance, insect resistance, general health, and deformities (Specification, page 21, lines 14-20). The growth data was analyzed using a best linear unbiased prediction software called GAREML (Dr. Dudley Huber, University of Florida, Gainesville, Florida) that generated breeding values for growth rate for the maternal parent and for every individual progeny (Specification, page 21, lines 14-20). Accordingly, applicants respectfully submit that no undue experimentation is required by one of ordinary skill in the art for make phenotype determinations in a multitude of tree species.

i. Additional Arguments Submitted by the Examiner

The Examiner states that Staub et al. (1996) *HortScience* 31(5):729-40 teach that phenotypic evaluation is unpredictable (Office Action mailed April 20, 2004, pages 6-7). Applicants respectfully disagree with the Examiner's characterization of Staub et al. First, Staub et al. do not disclose or suggest that phenotypic evaluation in plant breeding is unpredictable. In fact, applicants note that the determination of plant phenotypes is standard in any plant breeding method.

Second, Staub et al. discuss the use of morphological traits as genetic markers and phenotypic selection in the context of marker-assisted selection (Staub et al., page 729, Column 2, first full paragraph; page 737, Column 2, first full paragraph). As explained in the preceding section, marker-assisted selection links DNA markers with phenotypic traits. For example, Staub et al. state that "[m]orphological traits controlled by a single locus can be used as genetic markers if their expression is reproducible over a range of environments" (Staub et al., page 729, Column 2, first full paragraph). Genetic linkage between a marker and a trait implies a causal relationship between that marker and that trait. In contrast, and contrary to the Examiner's

continued assertions, applicants' invention does not encompass marker-assisted selection but uses DNA analysis merely to determine which of the plurality of parental trees represented in the polymix cross gave rise to a specific progeny tree. The presence of a particular polymorphic allele of a marker in both a parental tree and its progeny does not imply a relationship between that marker and any particular phenotypic trait that may be exhibited by both the parental tree and the progeny tree. In other words, just because a trait is observed in two trees, and both these trees also have the same polymorphic allele of a marker does not mean that that the marker and the trait are linked. Therefore, Staub et al. do not support the Examiner's position that phenotype determination in trees is unpredictable. Accordingly, applicants submit that the specification provides adequate guidance on phenotype determination in a multitude of tree species.

(C) The Use of Polymix Breeding Coupled With Pedigree Analysis to Select an Elite Breeding Group Requires no Undue Experimentation

The Examiner takes the view that the specification provides no guidance regarding the use of the claimed method to select elite genotypes, or the use of the method in any tree species other than *Pinus taeda* (Office Action mailed January 2, 2003, page 5; Office Action mailed August 27, 2003, page 5). In particular, the Examiner states that applicants have not actually demonstrated the reduction to practice of the claimed invention as it relates to the selection of actual elite trees (Office Action mailed October 18, 2004, page 7). Applicants respectfully disagree.

Applicants submit that the specification provides specific guidance for selecting elite trees from the progeny. For example, candidate plants are identified from the progeny plants based on having at least one phenotypic characteristic that is statistically better, based upon objective criteria than other progeny plants (Specification, page 13, lines 31-35). The specification describes examples of plant phenotypic traits that are commonly assayed, as well as methodology to assess the statistical significance of a phenotypic score (Specification, page 13,

lines 20-35). The pedigree of the progeny plants is determined using DNA analysis, and an elite breeding group is chosen based on high phenotypic scores and low levels of offspring relatedness. Moreover, the specification provides guidance for selecting elite trees from the progeny, for example, at page 16, line 19, to page 17, line 4. In some embodiments, elite plants are selected from the progeny plants based upon a characteristic selected from the group consisting of phenotype score, estimated breeding value, paternal breeding value, maternal breeding value and any combination thereof (see Specification, page 9, lines 27-30). For example, an elite plant that has a high phenotype score and has parents that are of high breeding value is particularly valuable as a breeding parent in the next generation. Knowledge of an elite plant's pedigree allows selection of the next generation of parental plants to maximize the genetic diversity of new breeding groups (see Specification page 16, lines 19-26). For example, in one embodiment, "[e]lite plants are selected by determining that the fathers of the candidate plants have an acceptable GCA and an acceptable level of relatedness" (Specification, page 16, line 35, to page 17, line 2). Example 4 shows that 29 out of 45 elite trees were determined to be paternally unrelated (Specification, page 22, lines 7-12; Table 3). Therefore, applicants submit that the specification provides adequate guidance on the use of polymix breeding coupled with pedigree analysis to select an elite breeding group

i. Additional Arguments Submitted by the Examiner

a. Stoehr et al. (1998) *Can. J. Forest Res.* 28(3):418-26 and Strauss et al. (1992) *Can. J. For. Res.* 22:1050-61: The Examiner states that Stoehr et al. teach that "environmental effects on trait expression may confound the selection of desirable progeny which should possess heritable genetic components conferring the phenotypic change" (Office Action mailed January 2, 2003, page 5). The Examiner also cites Strauss et al. as teaching that marker-assisted selection in tree breeding is unpredictable (Office Action mailed January 2, 2003, page 6). The Examiner

maintains that the claimed invention is directed to the correlation of DNA marker data and particular traits. Once again, applicants emphasize that their claimed method is not directed to any form of marker-assisted selection in tree breeding. Applicants' invention is *not* directed to linking DNA markers with one or more phenotypic traits. Instead, DNA analysis is used merely to determine which of the plurality of parental trees represented in the polymix cross gave rise to a specific progeny tree. Therefore, the references cited by the Examiner as teaching the unpredictability of marker-assisted breeding are inapplicable to applicants' claimed invention.

b. White (1996) *Proc. QFRI-IUFRO Conf. Tree Improvement for Sustainable Tropical Forestry*, pp. 110-117: The Examiner cites White as teaching that open pollination is unpredictable (Office Action mailed April 20, 2004, page 7) and that this unpredictability is applicable to polymix breeding (Office Action mailed October 18, 2004, page 4). Applicants respectfully point out that their invention is not directed to a breeding method using open pollination (*i.e.*, a pollination method in which a tree can be pollinated with pollen from any source). Instead, applicants' inventive method uses polymix breeding in which a mixture of pollen obtained from a defined breeding group of trees is used to pollinate a defined group of trees. Moreover, the White reference refers to potential issues for open pollination related to tropical species of trees compared to control pollination (see White, page 113, Column 1, second paragraph), and does not state that polymix breeding is unpredictable. In fact, rather than supporting the unpredictability of polymix breeding of trees, White states:

> Half-sib mating designs (including *polymix* and OP families when the OP families approximate half-sib families) are optimal or very nearly optimal over a broad range of conditions for both estimating heritabilities and g x e and also for ranking parents (and hence maximising gain from backward selection) (White, page 111, Column 1, paragraph 2, emphasis added).

Accordingly, White does not support the Examiner's position that polymix breeding is unpredictable. Based on the Examiner's reasoning, open-pollinated breeding would be even less

predictable than polymix breeding given that the potential pollen contributors are not fully known, as they are with polymix breeding. On the contrary, it has been found that open-pollination breeding gives good estimation of parental breeding values and heritability estimates (Specification, page 3, line 33, to page 4, line 5). Moreover, simulation studies have shown that polymix breeding with no parental analysis can provide genetic gains nearly as good as those achieved using full-sib (full-pedigree) systems (Specification, page 6, lines 10-18).

c. Wiselogel & Buijtenen (1988) *Silvae Genetica* 37(5-6):184-7; Rogers & Boyle (1991) *Heredity* 67:373-79; and Moran & Griffin (1985) *Silvae Genetica* 34(4-5):117-21: The Examiner cites Wiselogel & Buijtenen, Rogers & Boyle, and Moran & Griffin as teaching that the use of polymix breeding may be confounded by the unequal reproductive success of many parents' pollen (Office Action mailed January 2, 2003, page 6). As an initial matter, applicants point out that, contrary to the Examiner's assertion, polymix breeding provides excellent estimation of breeding value and general recombining ability (Specification, page 6, lines 2-6). Indeed, Moran & Griffin conclude that, despite evidence of non-random contribution of pollens to viable seed formation, "such effects are not so strong as to affect the utility of the polymix mating design in practical tree breeding" (Moran & Griffin, page 121, Column 1, last paragraph). Moreover, equal fertilization success of the pollen parents of the premix is not essential to the success of the methods of the invention. Notably, the claimed method actually serves to overcome any effect of unequal pollination through pedigree analysis, thereby allowing for more predictable polymix breeding programs (see Specification, page 7, line 34, to page 8, line 12).

d. Lambeth et al. (2001) *Theor. Appl. Genet.* 103:930-43: The Examiner cites Lambeth et al. as teaching that the claimed process is unpredictable (Office Action mailed August 27, 2003, page 4; Office Action mailed April 20, 2004, page 7; Office Action mailed October 18, 2004, page 4). Applicants respectfully disagree with the Examiner's conclusions. As an initial

matter, applicants note that Lambeth et al. is a publication by the inventors describing one of the embodiments of the invention. It does not constitute prior art because it was published after the filing date of the present application.

According to the Examiner, Lambeth et al. admit that the success observed by them was dependent on a particular breeding population and a small number of markers (Office Action mailed April 20, 2004, page 7). Applicants respectfully disagree. First, Lambeth et al. describes 3 cases out of 45 in which the observed genotypes were not consistent with the expected genotypes (Lambeth et al., page 936, Columns 1-2). Rather than showing that the process is unpredictable, these results indicate that in more than 93% of cases the expected result was obtained. Second, Lambeth et al. attribute the *failures* rather than the *successes* to the breeding population–specifically, the considerable relatedness of the breeding population–and the small number of markers used (Lambeth et al., Abstract). Moreover, Lambeth et al. point out that these inconsistencies could have arisen due to an inaccurately labeled pedigree, which is known to occur with a higher than acceptable frequency in tree breeding and which could be avoided by the routine use of markers in confirming parentage in progeny tests (Lambeth et al., page 936, Column 2). Finally, Lambeth et al. note that "[t]he inclusion of more markers and/or the creation of polymixes and breeding groups that avoid relatedness would resolve this problem" (Lambeth et al., Abstract; see also Specification, page 19, line 30, to page 20, line 2). Therefore, Lambeth et al. do not support the Examiner's conclusion that the claimed process is unpredictable.

e. Other Argument: The Examiner states that "the exemplified pine species has unique characteristics which make it uniquely suited to the claimed process" (Office Action mailed April 20, 2004, page 6). However, the Examiner fails to identify any of these "unique characteristics."

Conclusion

In summary, applicants respectfully submit that the specification contains specific guidance on the identification of genetic polymorphisms from a variety of tree species to enable the determination of the pedigree of progeny trees by DNA analysis. In addition, numerous other genetic polymorphisms in trees were well known in the art at the time of filing this application for many tree species, as noted above. As pointed out by the Federal Circuit, "a patentee preferably omits from the disclosure any routine technology that is well known at the time of application." *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254, 70 U.S.P.Q.2d 1321, 1325 (Fed. Cir. 2004). The specification also provides sufficient guidance on phenotype determination in tree species. Moreover, the determination of plant phenotypes is standard in plant breeding methods. Finally, the specification also provides sufficient guidance regarding the use of the claimed method to select elite genotypes. Therefore, applying the *Wands* factors to the instant application, it is apparent that a reasonable correlation exists between the scope asserted in the claimed subject matter and the scope of guidance the specification provides because the specification contains adequate, specific guidance on the identification of markers from a variety of tree species and use of the markers in a polymix breeding program. The specification contains a working example using the method of the invention to generate candidates for an elite group, and guidance is provided on the selection of an elite breeding group.

As stated by the predecessor court to the Federal Circuit, it "is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is consistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). The reasoning provided and the references cited by the Examiner in this case do not support the position that undue

experimentation is required to practice the claimed invention. Accordingly, the Examiner has failed to establish a *prima facie* case of non-enablement of Claims 20-31. Applicants respectfully request reversal of this ground of rejection.

3. Rejection Under 35 U.S.C. § 103(a)

Claims 20-31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bridgwater (1992) in *Handbook of Quantitative Forest Genetics*, Kluwer Academic Pub., Dordrect, The Netherlands, pp. 69-95, in view of El-Kassaby & Ritland (1992) *Theor. Appl. Genet.* 83(6-7):752-8 and Stoehr et al. (1998) *Can. J. For. Res.* 28:187-95. According to the Examiner, it would have been obvious to one of ordinary skill in the art to utilize the method of polymix tree breeding taught by Bridgwater and to modify that method by utilizing the pedigree analysis step in the Douglas fir polymix breeding program taught by El-Kassaby & Ritland and to further modify that method by utilizing the DNA marker taught by Stoehr et al. Applicants respectfully disagree.

Three basic criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. Manual of Patent Examining Procedure (M.P.E.P.) (8th ed. Aug. 2001; rev. May 2004) § 2143. Moreover, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. § 2141.02. (emphasis in original). *See also W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

The Federal Circuit has consistently held that a person of ordinary skill in the art must not only have had some motivation to combine the prior art teachings, but some motivation to

combine the prior art teachings in the particular manner claimed. *See, e.g., In re Kotzab*, 217 F.3d 1365, 1371, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000) ("Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."); *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998) ("In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.").

For the reasons set forth in detail below, applicants respectfully submit that the burden of establishing a *prima facie* case of obviousness has not been met because there is no suggestion to combine or modify the reference's teachings to arrive at the claimed invention.

Applicants respectfully submit that Bridgwater does not teach or suggest step (d) determining the pedigree of a plurality of progeny trees using DNA analysis or step (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20, from which Claims 21-31 depend. Instead Bridgwater simply provides a review of different types of mating designs used in breeding programs, including polymix breeding. Bridgwater provides no suggestion or motivation to either use DNA analysis to determine the pedigree of progeny trees, as recited in step (d) of Claim 20, or to use a pedigree and a phenotype score to identify elite trees, as recited in step (e) of Claim 20. Moreover, applicants submit Bridgwater teaches away from the use of polymix breeding by stating that "[i]f there is strong variation for general combining ability among males and inbreeding depression is present, selection in base populations produced from polycross matings will reduce expected gains since most selections may be progenies of the same few pollen parents" (Bridgwater, page 75, first full paragraph). As further described below, neither El-Kassaby & Ritland nor

Stoehr et al. provide any motivation or suggestion to modify the teachings of Bridgwater to arrive at the claimed invention.

Applicants submit that El-Kassaby & Ritland do not teach or suggest any of the steps of (c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score, (d) determining the pedigree of a plurality of progeny trees using DNA analysis, or (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20. El-Kassaby & Ritland describe a study of male reproductive success using a polymix of three pollen donors, in which the paternity of progeny was determined based on four protein markers (El-Kassaby & Ritland, page 753, Column 2). El-Kassaby & Ritland provide no suggestion or motivation to use their method of determining paternity in a tree breeding program. Specifically, there is no suggestion or motivation in El-Kassaby & Ritland to determine the pedigree of progeny trees using DNA analysis and using the pedigree information as well as a phenotype score to identify elite trees.

Similarly, applicants submit that Stoehr et al. do not teach or suggest the steps of (c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score or (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20. Rather, Stoehr et al. use a polymorphic genome marker to estimate the level of outside-orchard pollen contamination, supplemental mass pollination efficacies and natural selfing in Douglas fir (Stoehr et al., Abstract). Stoehr et al. provide no motivation or suggestion to use their method in a tree breeding program. Specifically, there is no suggestion or motivation in El-Kassaby & Ritland to use pedigree information as well as a phenotype score to identify elite trees.

Therefore, none of the references cited by the Examiner, alone or in combination, teach or suggest the steps of the claimed invention. In particular, none of the references teach or suggest

the step of (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding. For the reasons noted above, the cited references fail to teach, suggest, or provide any motivation to make or otherwise render obvious the claimed invention. Accordingly, applicants respectfully request reversal of this ground of rejection.

VIII. CLAIMS APPENDIX

1-19. (Canceled)

20. (Original) A tree breeding method comprising:

(a) mixing pollen obtained from a breeding group comprising a plurality of parental trees to obtain a pollen polymix;

(b) pollinating female reproductive structures from each parental tree in the plurality of parental trees with the pollen polymix to obtain a plurality of progeny lots, wherein each progeny lot comprises seeds obtained from a different cross between the pollen polymix and each different parental tree of the plurality of parental trees;

(c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score;

(d) determining the pedigree of a plurality of progeny trees using DNA analysis; and

(e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding.

21. (Previously presented) The method of Claim 20 additionally comprising selecting candidate trees from within the progeny trees based upon their phenotype score, wherein step (d) is performed on the candidate trees, and step (e) is performed using the pedigree and phenotype scores from the candidate trees to identify elite trees for use in a next generation of plant breeding.

22. (Previously presented) The method of Claim 20, wherein the pedigree and phenotype scores are used to estimate the breeding values of a plurality of progeny and parental trees, and the breeding values are used to identify the elite trees for use in a next generation of breeding.

23. (Previously presented) The method of Claim 22, wherein the elite plants are derived from parental plants that have a high general combining ability.

24. (Previously presented) The method of Claim 20, wherein the pedigree determined is paternity.

25. (Previously presented) The method of Claim 20, wherein the pedigree determined is paternity and maternity.

26. (Previously presented) The method of Claim 20, wherein the phenotype score is obtained for a phenotype selected from the group consisting of disease resistance, growth rate, growth habit, chemical composition of any plant tissue, drought resistance, temperature hardiness, elevation adaptation, fecundity, and any combination thereof.

27. (Currently amended) The method of Claim 20, wherein the DNA analysis is performed using a DNA analysis method selected from the group consisting of DNA sequencing, restriction fragment length polymorphism (RFLP), amplified fragment length polymorphism (AFLP), randomly amplified polymorphic DNA (RAPD), single nucleotide repeat microsatellites ~~(i.e., simple sequence repeats (SSR))~~, di-, tri-, and tetra-nucleotide repeat SSRs, SSR-anchored PCR, sequenced tagged sites (STS), single nucleotide polymorphism (SNP), single stranded conformational polymorphism (SSCP), sequenced characterized amplified regions (SCAR), allele-specific associated primers (ASAP), single primer amplification reaction (SPARs), and cleaved amplified polymorphic sequences (CAP).

28. (Previously presented) The method of Claim 20, wherein a plurality of pollen polymixes are prepared, each pollen polymix comprised of pollen obtained from a plurality of different parental trees, each pollen polymix of the plurality of pollen polymixes being used to pollinate female reproductive structures from parental trees whose pollen or that of its close relatives are not represented in the pollinating pollen polymix.

29. (New) The method of Claim 27, wherein the DNA analysis method is performed using single nucleotide repeat microsatellite analysis.

30. (New) The method of Claim 20, wherein the breeding group consists of conifer species.

31. (New) The method of Claim 30, wherein the DNA analysis method is performed using single nucleotide repeat microsatellite analysis.

IX. EVIDENCE APPENDIX

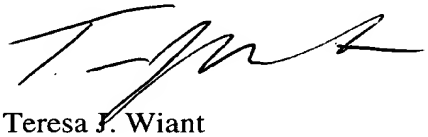
None.

X. RELATED PROCEEDINGS APPENDIX

None.

Respectfully submitted,

WEYERHAEUSER COMPANY



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